

REMARKS

Claims 52-55, 57-66, and 68-73 are pending. In the near future, applicants will file a Declaration by an expert in the field to further support the following remarks.

Double Patenting Rejection

In the Office Action mailed February 1, 2002, the Examiner maintains the rejection of Claims 52-55, 57-66, and 68-73 under the judicially created doctrine of obviousness-type double patenting as unpatentable over Claims 1-7 and 17-23 of U.S. Patent No. 5,854,205.

Applicants respectfully disagree with the Examiner's position that Claims 52-55, 57-66, and 68-73 are obvious in view of the above recited patent. However, to advance prosecution, applicants plan to file an appropriate terminal disclaimer in compliance with 37 C.F.R. §3.37(b) once allowable subject matter is found in the present application. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

The Examiner also maintains the provisional rejection of Claims 52-55, 57-66, and 68-73 under the judicially created doctrine of obviousness-type double patenting as unpatentable over Claims 1-8, 15-17 and 19-20 of co-pending Application No. 09/315,689.

Applicants respectfully disagree with the Examiner's position that Claims 1-8, 15-17 and 19-20 are obvious in view of Application No. 09/315,689, now U.S. Patent No. 6,346,510. However, to advance prosecution, applicants plan to file an appropriate terminal disclaimer in compliance with 37 C.F.R. §3.37(b) once allowable

subject matter is found in the present application. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Claim Rejections – 35 U.S.C. § 112, 1st paragraph

New Matter Rejection

The Examiner maintains the rejection of Claims 52-55 and 57-62 under a new matter rejection set forth under 35 U.S.C. § 112, first paragraph, for reasons of record in the Office Action issued on July 19, 2001 (hereinafter *Paper No. 9*). In *Paper No. 9*, the Examiner asserts that the claims read on any protein comprising an NC1 region or a fragment thereof, and that the specification as originally filed does not support this. Applicants respectfully disagree. Claims 52-55 and 57-62 are directed to an antiangiogenic fragment of an NC1 region of a collagen protein. Applicants respectfully assert that the specification conveys in a reasonable manner to one skilled in the art their possession of the invention – a genus of antiangiogenic fragments of a C-terminal non-collagenous (NC1) region of a collagen protein. Particularly, Examples 1-3 teach how to isolate antiangiogenic fragments from this region. The specification further provides a method for evaluating antiangiogenic activity using assays such as the CAM assay (page 40, lines 1-21, of applicants' specification).

In view of the foregoing, applicants respectfully assert that the invention as claimed is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed, had possession of the claimed invention. Therefore, applicants request the withdrawal of the rejection.

Enablement

The Examiner maintains the rejection of Claims 52-55, 57-66 and 68-73 under 35 U.S.C. § 112, first paragraph, for scope of enablement for reasons set forth in *Paper No. 9*. The Examiner asserts that the specification does not reasonably provide enablement for a protein comprising or consisting of any fragment of NC1. Applicants respectfully traverse the rejection.

Applicants assert that the present claims are directed to a fragment of a NC1 region of a collagen protein which inhibits angiogenesis. Applicants have defined such fragments according to both structure and function, and, based on applicants' description together with the level of knowledge in this field at the time the application was filed, one skilled in the art would easily be able to identify antiangiogenic fragments derived from collagen proteins. The structural feature of importance is the C-terminal noncollagenous region (NC1) of collagen proteins. The NC1 region is a structural feature of a collagen protein well-known in the art at the time of the invention. The functional feature of importance is the antiangiogenic activity. The present specification provides a detailed "roadmap" for discovering additional antiangiogenic fragments of a NC1 region of a collagen protein. Particularly, Examples 1-3 teach how to isolate antiangiogenic fragments from this region. The specification further provides a method for evaluating antiangiogenic activity using assays such as the CAM assay (page 40, lines 1-21, of the applicants' specification). Because the NC1 regions are defined, the specification enables one of skill in the art to use fragments of this region as a method of inhibiting angiogenesis.

In view of the foregoing, applicants respectfully reassert their position that the specification enables the genus of the anti-angiogenic fragments of the NC1 domain of collagen proteins. Applicants request withdrawal of the rejection.

Written Description

The Examiner maintains the rejection of Claims 52-55, 57-66 and 68-73 under 35 U.S.C. 112, first paragraph for reasons of inadequate written description for reasons set forth in *Paper No. 9*. Applicants respectfully traverse the rejection.

Applicants respectfully assert that the present specification allows one skilled in the art to clearly see what is claimed. The specification has provided a detailed "roadmap" for discovering additional species beyond the two explicitly described species (collagen XV and collagen XVIII within the genus). The structural features of collagen molecules (right-handed type triple helices as the collagenous regions and terminal portions as the noncollagenous regions) are well known in the art. The Examiner cites the lack of homology between collagen XV and collagen XVIII sequences and lack of guidance regarding specific amino acid sequences of NC1-region fragments to support the rejection. Applicants respectfully assert that the collagens comprise a large family of *genetically* distinct, but *structurally* related proteins. A prominent and common feature of most of the collagens is that they contain both collagenous and noncollagenous regions. Those skilled in the art easily recognize the highly conserved features of collagens consisting of right-handed triple helices as the collagenous regions, and intervening areas and terminal portions as the non-collagenous regions. Lack of sequence similarity between non-collagenous regions of different collagen proteins would not prevent one skilled in the art from

recognizing them as such, given general level of knowledge in the art regarding the structure of whole collagen molecule. Therefore, given applicants' teaching of NC1 domains, their location and methods for identifying antiangiogenic activity, together with the level of knowledge of collagen molecule structure at the time of applicants' priority date, a skilled artisan could reasonably identify potential antiangiogenic fragments from C-terminal NC1 regions of collagen proteins without relying on information concerning amino acid sequences or homology to previously identified antiangiogenic fragments.

Applicants respectfully submit that a combination of applicants' teaching of NC1 domains, their location, and methods for identifying antiangiogenic activity, together with the level of knowledge of those skilled in the art at the time of applicants' priority date, would enable a skilled artisan could reasonably identify potential antiangiogenic fragments from C-terminal NC1 regions of collagen proteins. Therefore, applicants reassert their position that the invention as claimed is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed, had possession of the claimed invention, and applicants request the withdrawal of the rejection.

Claim Rejections – 35 U.S.C. § 102(e)

The Examiner maintains the rejection of Claims 52-54 and 57-62 under 35 U.S.C. §102(e) as anticipated by to *Olsen et al.* (U.S. Patent No. 5,643,783). Applicants respectfully traverse the rejection. *Olsen et al.* discloses the amino acid sequence of the **entire** collagen type XVIII. The present claims are directed to an antiangiogenic fragment of an NC1 region of a collagen protein. *Olsen et al.* fails to

teach or suggest antigiangiogenic properties of an NC1 region of a collagen protein. Therefore, *Olsen et al.* fails to anticipate the claims. In view of the foregoing, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

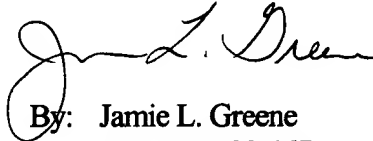
The foregoing is submitted as a full and complete response to the Final Office Action mailed on February 1, 2002. Applicants assert that the claims are now in condition for allowance and respectfully request that the application be passed to issuance. If the Examiner believes that any informalities remain in the case which may be corrected by Examiner's amendment, or that there are any other issues which can be resolved by a telephone interview, a telephone call to the undersigned attorney at (404) 815-6500 is respectfully solicited.

Application Serial No. 09/405,499
Title: Endostatin Protein And Fragments Thereof
Response to Office Action
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No additional fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies which may be required or credit any overpayment to Deposit Account Number 11-0855.

Respectfully submitted,

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